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10/650,280	08/27/2003	Kenneth W. Wood	UCSD-07982	6632

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,280	WOOD ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/27/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment filed 8/27/2003 is acknowledged. Claims 1-16 and 36-42 were canceled.

Claims 17-35 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

2. Claims 17-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite because of the abbreviation "CENP-E". An abbreviation must be accompanied by the full name at its first occurrence in the claims.

3. Claims 26-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is that claimed methods drawn to identifying lead therapeutic compounds, lead bioagricultural compounds or lead diagnostic compounds are not enabled by the specification, because the specification fails to teach how to use CENP-E modulators for the purposes of therapy, uses in bioagriculture or in diagnosis of a disease.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claimed inventions are drawn to methods for identifying modulators of CENP-E activity, where the activity is selected from plus end-directed microtubule motor activity, ATPase activity and microtubule binding activity; where the modulators will be used as therapeutic compounds, bioagriculatural compounds or as diagnostic agents. Therefore, the claimed inventions are based on an assumption that modulating CENP-E activity would be useful in a method of therapy, in bioagriculture or in the diagnosis of a disease.

The specification provides prophetic teachings concerning the use of CENP-E modulators as useful in therapy, bioagriculture or diagnosis. For example, the specification provides a laundry list of human and animal diseases on page 41-42 (bridging paragraph).

The prior art fails to teach any association between a CENP-E activity and a disease state, or a bioagricultural use or a diagnosis of a disease. The specification also fails to provide a nexus between a specific disease, or bioagricultural use of a CENP-E modulator.

The nature of the claimed inventions is such that in addition to providing an assay method, the practice the invention one must be aware of a specific association between CENP-E and a disease state or a bioagricultural application. In the instant case, the specification fails to

provide guidance for such an association, but instead provides teachings indicating a future potential application of the claimed methods.

Thus, the claimed inventions are not enabled because further experimentation would have to be done to practice the claimed inventions. This further experimentation is undue experimentation because one of skill in the art would have to engage in experimentation to discover an association between a disease or a bioagriculture application, which experimentation is not routine experimentation.

4. Claims 17-21 and 23-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying a candidate agent that modulates CENP-E activity, where CENP-E is characterized by SEQ ID NO, does not reasonably provide enablement for mfor methods of identifying candidate agents that modulate any and all proteins characterized only by the term "CENP-E". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The disclosure of the specification does not contain an adequate written description, examples, or guidance whereby, methods of identifying candidate agents that modulate CENP-E activity where CENP-E is characterized only as "CENP-E" could be placed into the hands of the skilled artisan with a reasonable expectation of success without requiring undue experimentation.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence

or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The specification defines the scope of the term "CENP-E" or "human CENP-E" or Xenopus CENP-E (XCENP-E) as possibly having at least 34% sequence identity to SEQ IDNO: 1. In altenative embodiments CENP-E maybe form fungus, insects, or plants. Therefore, the claims read on methods for discovering candidate agents that modulate variants of "CENP-E" or "human CENP-E" or "Xenopus CENP-E", such variants including, for example, deletions from, or insertions or substitutions of residues within "CENP-E" or "human CENP-E" or "Xenopus CENP-E".

However, the study of the relationship between the primary amino acid sequence and protein function is highly unpredictable. Bowie et al (Science, 247: 1306-1310, 1990) teaches that while it is known that many amino acid substitutions are possible in any given protein, the position with the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Burgess et al (J. Cell Biology, 111 : 2129-2138, 1990) teaches that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al (Molecular and Cellular Biology, 8: 1247-1252, 1988) teaches that replacement of aspartic acid at position 47 with alanine or asparagines does not affect biological activity while replacement with serine or glutamic acid sharply reduces the biological activity of the protein. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and

characteristics of a protein. Because of the unpredictability of the protein arts, the skilled artisan cannot make and use the broad genus of methods that involve the use of "CENP-E" or "human CENP-E" or "Xenopus CENP-E" recited in the claims because such a genus encompasses proteins having an unlimited and thereby infinite plurality of amino acid substitutions, deletions, additions, or combinations thereof, as compared with the working embodiments.

The instant method claims encompass methods for identifying modulators of the activity of all types and manner of "CENP-E" or "human CENP-E" or "Xenopus CENP-E", which is not characterized by amino acid sequence. The specification appears to broadly define CENP-E "to include CENP-E from practically every animal species on earth and every possible allelic variant of the foregoing, which variants are not envisioned or adequately described by the disclosure. The working embodiments of the specification provide assays for a single protein, that of a protein having the motor domain defined as the amino acid sequence of SEQ ID NO: 1, which is a minor portion of a very broad genus of proteins encompassed by the term "CENP-E", and does not teach or support the majority of the genus as a whole. One of skill in the art would have to engage in further experimentation to learn how to use many of the claimed methods. Therefore, such further experimentation would be undue experimentation, because it would constitute experimentation on the claimed invention to discover uses and the biological function of a broad range "CENP-E" proteins, and variants thereof.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 17-19, 23, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Lombillo (Lombillo, V. et al., The Journal of Cell Biology, 128(1&2): 107-115, 1995; cited in the IDS).

The claimed inventions are drawn to methods of identifying candidate agents as modulators of CENP-E activity comprising at least one activity selected form the group consisting of plus end-directed microtubule motor activity, ATPase activity, and microtubule binding activity. Claim 18 requires that the method comprising the step of isolating biologically active CENP-E from a cell sample. The specification fails to teach the degree of isolation. Therefore, isolation of chromosomes from a cell sample is encompassed by isolation of CENP-E from a cell sample because CENP-E is associated with chromosomes (see abstract).

Lombillo teaches a method for identifying antibodies that modulate CENP-E dependent microtubule depolymerization-driven chromosome motion (which reads on "microtubules motor activity") on page 108 and page 111-112, bridging paragraph. Thus, Lombillo teaches methods that are the same as that claimed.

6. Claims 17-19, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Thrower (Thrower, D.A., et al, The EMBO Journal, 14(5): 918-926, 1995; cited in the IDS).

The specification fails to teach the degree of isolation of CENP-E. Thus, D-100 extracts are interpreted to be encompassed by isolated CENP-E.

Thrower teaches a method for determining nucleotide specificity and inhibitor specificity of microtubule movement due to human CENP-E in a D-100 mitotic extract (see 924-925 and page 920). Thus, Thrower teaches methods that are the same as that claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 17, and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lombillo (supra) in view of Duesbery (Duesbery, N.S. et al. Proc. Natl. Acad. Sci., USA, 94: 9165-9170, 1997, August; cited in the IDS).

Claims 17 and 20-22 include within their scope methods where the CENP-E activity is Xenopus CENP-E activity. The specification teaches that an inherent feature of Xenopus CENP-E activity is that it comprises the structure of SEQ ID NO: 1 (motor domain).

Lombillo teaches as described above. Lombillo fails to teach methods where the CENP-E activit is that of Xenopus CENP-E activity. However, Xenopus CENP-E is known in the art as evidenced by the teachings of Duesberry (see page 9166, 1st and 2nd column). Duesberry teaches immunoprecipitation of Xenopus CENP-E, and Duesberry teaches an antibody specific for Xenopus CENP-E, and also teaches that an antibody specific for human CENP-E also binds to Xenopus CENP-E. Thus, it would have been prima facie obvious to have used the chromosomes isolated from Xenopus eggs as taught by Duesberry in the method of Lombillo to make a method that comprised testing for modulators of Xenopus CENP-E activity. One would have been motivated to have used Xenopus CENP-E because Duesberry teaches an antibody to the tail of Xenopus CENP-E and one would have been able to use this antibody to determine the role of the tail portion of the CENP-E in CENP-E function.

8. Claims 17 and 35 are rejected under 35 U.S.C. 103(a) as being obvious over Lombillo (supra) or Thrower (supra) in view of Jubin (US 5,759,795; issued 6/2/1998; effective filing date 3/8/1996).

Claims 17 and 35 include within their scope methods where a plurality of candidate compounds are tested. Neither Lombillo nor Thrower explicity teach simultaneous screeninig methods. However, high-throughput screening methods are known in the art as evidenced by the teachings of Jubin for detection of inhibitors of ATPase activity. Jubin teaches that use of high throughput screening is useful for screening multiple candidate compounds for ATPase activity. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Lombillo or Thrower to look for antibodies or nucleotides that inhibited ATP activity in CENP-E using the high throughput screening method of Jubin.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official

Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
June 24, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER